The Nature of the Albuminuria of Bright's Disease.

SEMMOLA, of the University of Naples, has recently communicated the results of his last researches on this subject to the Academy of Medicine, of Paris. It is now quite well established that the term "Bright's disease" is defective, and should only be considered as a general term under which different lesions of the kidney may be grouped, differing in seat and in the nature of their processes. Formerly the different lesions observed in the kidney were considered as the successive phases of the same disease; at present no one retains this idea. The name "Bright's disease" should be reserved for permanent, chronic albuminuria, for diffuse parenchymatous nephritis. What first produces the passage of albumen into the urine? Gubler, Jaccoud, and Semmola hold that the origin of the disease is in an altered state of the blood. Under some special influence the albumen of the blood is altered or increased, and then becomes capable of passing through the glomeruli. Others, as Dujardin-Beaumetz, hold at the same time to an alteration of the blood and some lesion of the kidney as the cause.

In his latest researches Semmola has endeavoured to show that the passage of albumen through the kidney presupposes no real lesion, but that this is a result; that the albumen of the various albuminuriæ cannot be distinguished chemically, whilst a high degree of diffusibility of albumen always denotes true Bright symptoms; that the bile of Bright subjects contains albumen; that the saliva and perspiration also contain it; and that the primary cause of the affection should be sought for in some alteration of the nutritive functions of the skin. He thinks that experimental facts fully justify this theory.

The experimenter has endeavoured to reproduce as nearly as possible the processes involved in Bright's disease. With this view he has suddenly introduced a large quantity of albumen into the blood, and has cautiously injected white of egg, in small quantities at first, into the subcutaneous tissue of dogs, which were kept under its influence for more than twenty days. He has kept dogs under its influence for thirty days, making daily injections of f℥ijss to more than f℥ij of white of egg. After four or five days the kidneys become congested, and if the quantity injected be large renal hemorrhage occurs. After seven or eight days leucocytes appear, and fatty degeneration of the epithelium sets in; and after fifteen days the kidney commences to get fatty. If the experiment is kept up, toward the twenty-fourth day the lesions of the kidney are almost identical with those of interstitial nephritis. The introduction of albumen into the blood causes an albuminuric dyscrasia, as shown by the fact that the quantity of albumen eliminated is greater than that injected. The bile becomes charged with albumen, and Semmola thinks that he is authorized in stating that he has realized artificially the natural morbid process. But the facts here show that the albuminuria is the primary, and the renal lesion the secondary lesion.

As to the primary cause of albuminuria, Semmola is convinced that it must be sought in some alteration of the nutritive functions of the skin.

In making the experiments he used different albuminous substances, as serum of blood, yolk of egg, and milk. With these the effects were different from those caused by white of egg injections. With blood serum the renal process was less rapid, and no functional alteration was caused by injections of yolk of egg and milk.—*Revue Méd. Franç. et Étrang.*, June 9, 1883.

Semmola has been convinced for three years, after a long experience, of the many imperfections in the chemical reactions for differentiating the different kinds of albumen. He has, therefore, turned his attention to the degrees of diffusibility of the albuminoids of the blood in the different albuminuriæ, and he is convinced that the great secret to be studied lies in the different gradations of the albuminoids by reason of their diffusibility, or, in other words, their aptitude for performing their functions in the nutritive processes; and has arrived at the following conclusions:—

1. The albuminoids of the blood of Bright subjects are much more diffusible than the albuminoids of the blood in other kinds of albuminuria (mechanical albuminuria).

2. In Bright subjects of the first stage, and therefore curable, if the blood serum is examined before and after recovery, it is seen that the diffusibility of the blood albuminoids augments, diminishes or ceases in perfect relation with the quantity of albumen eliminated by the urine. Hence it is evident that the degree of diffusibility of the blood albuminoids constitutes the true point of departure of the albuminuria of Bright's disease.

3. This physico-molecular constitution of the blood albuminoids which characterizes their non-assimilability, and which consequently causes their forced elimination, is caused by a defect, greater or less, of the cutaneous functions. In support of this view Semmola brings forward a number of laboratory experiments and clinical observations which clearly prove the relation existing between the activity of the cutaneous functions and the alteration of the diffusibility of the blood albuminoids, or their degree of assimilability. He examines, by comparison, the degree of diffusibility of the blood albuminoids before and after varnishing the skin over a more or less extended portion, so that the animal may live a sufficient time. He has found that, all things being equal, the blood serum of these animals presents at least one-third of the principal albuminoid principles which become diffused if the varnishing occupies so much as one-half of the cutaneous surface. In these cases albuminuria is also seen, and the bile of these animals contains albumen in the proportion of three to five in one thousand.

As to the clinical observations, he has collected a series of cases of chronic eczema and psoriasis which alternated in their appearance on the skin with albuminuria, and which were finally cured by a long hydrosudopathic treatment. He relates one case of cutaneous seborrhœa in which the skin perfectly reproduced the experiment of the varnished dog. Water did not moisten it, and the patient was always cold; for a long time he felt the least breath of air, and became profoundly cachectic. He had albuminuria, and it was only after a long course of hydrosudopathy that he was completely cured; the albuminuria never reappeared.

Semmola thinks, therefore, that it is incontestable that the first stage of Bright's disease is constituted by a profound modification of the albuminoids of the blood which succeeds in proportion to the progressive enfeeblement of the respiratory functions of the skin, under the influence of cold and moisture, which are, in his opinion, the fundamental causes of true Bright's disease. This action of damp cold is very slow, and Bright subjects are already victims of the disease before they are aware of it. At this period there already exist the three characteristic symptoms of the disease in their order of sequence: 1. Increasing diffusibility of the principal blood albuminoids, and, consequently, increasing diminution of their assimilability. This chemical state he calls *etheralbuminuria*. 2. Diminution of the quantity of urea on the one hand, and, on the other, forced elimination of the albuminoids, by all the emunctories whose office is organic depuration, primarily the kidneys.

From these facts he was led to analyze the bile of Bright patients after death, and he found that the distinguishing feature of Bright albuminuria as compared with other albuminuriæ is, that on analyzing the bile *post-mortem*, albumen is found in the bile in the first case and not in the second. The sweat and saliva, artificially produced, present the same differences as regards the presence of albumen. The final conclusion which he draws is of great interest because it is grouped with the differences already noted in the different albuminuriæ. In the albuminuria of Bright's disease there is a loss of albumen which the organism produces through its different emunctories in order to rid itself of the albuminoids which have already become non-assimilable; and in the other varieties of albuminuria (mechanical, nephritic, etc.) elimination of the albumen is due to a purely local cause which depends either on the degree of pressure of the renal circulation or upon epithelial alterations.

To demonstrate this theory, built upon laboratory experiments and clinical observation, one step remained—the experimental demonstration that the non-assimilable albuminoids (and therefore foreign to the organism) are capable of producing a renal process analogous to that of Bright nephritis by the fact that they can pass through the renal filter; this Semmola has demonstrated by a long series of delicate and conclusive experiments. He injected albumen into the areolar tissue, and rejected the common experiment of injecting white of egg directly into the blood, being convinced that albumen injections into the blood cause troubles too profound to obtain a complete resemblance to *etheralbuminuria* or to *etheralbuminosis* caused naturally. He injected variable quantities of white of egg—from fʒv to f℥ijss daily—always keeping an accurate record of the weight of the animal in order to establish a constant relation between it and the amount of albumen injected. After the second day there gradually came on hyperæmia, sometimes simple, then accompanied by globular extravasation into the capsule, and even into the interior of the uriniferous tubules. The capsule was distended by an amorphous or granular material having the characteristics of albumen. Later, tumefaction appeared, migration of lymphoid cells, advanced fatty degeneration, epithelial necrosis, and even proliferation commencing in the areolar tissue in the animals which had for a long time resisted albuminous injections. In order to confirm these experiments they were repeated with other and less heterogeneous substances than white of egg—such as the yolk of egg, blood-serum, albumino-peptones, and milk.

Prof. Semmola does not think it necessary to give in detail the particulars of these comparative experiments; at present it suffices to say that the more the chemico-molecular constitution of the albumen approaches that of normal blood albumen, the less injurious will be its passage through the kidneys. Thus, injection of blood-serum into the subcutaneous areolar tissue is followed by albuminuria, but, other things being equal, it produces less slowly renal irritation, which is more feeble and transitory. He has observed, lastly, in dogs an albuminuria more or less developed in relation to the quantity of albuminoids injected, and more or less pronounced according to the degree of diffusibility of the albuminoids of the blood-serum. Anasarca never appears when small quantities are injected, although a minute quantity of albumen is eliminated by the kidneys. These facts also confirm, what Semmola has clearly shown, that the chemico-molecular constitution of the albuminoids of the living organism is of the greatest variability, and that a mere trifle, the simple passage through a living membrane, is capable of modifying them, and even rendering them non-assimilable, diffusible, in other words, and incapable of performing their functions in the work of nutrition. —*Progrès Méd.*, June 16, 1883.

Relation between Serum-Albumen and Globulin in Albuminuria.

This subject has been recently thoroughly investigated by Prof. F. A. HOFFMAN. He finds that ascitic fluid contains less albumen than the serum of blood. This is not extraordinary; albumen diffuses slowly through animal membranes,